AMENDMENTS TO THE CLAIMS:

Please amend claims 1, 50, 59, 61-65 and 141 as set forth below, cancel claims 58, 60 and 140 without prejudice or disclaimer, and add claims 144-147. This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method for introducing a large nucleic acid molecule into a cell, comprising:

(a) exposing ~~the~~ a large nucleic acid molecule to a delivery agent;

(b) exposing the cell to a delivery agent; and

(c) contacting the cell with the nucleic acid molecule, whereby the nucleic acid molecule is delivered into the cell, wherein steps (a)-(c) are performed sequentially in any order ~~or simultaneously~~, provided that if the delivery agent is energy it is not applied to the nucleic acid molecule and it is not applied to the cell after contacting the cell with the nucleic acid molecule.

Claim 2 (original): The method of claim 1, wherein:

the nucleic acid molecule is exposed to an agent that increases contact between the nucleic acid molecule and the cell; and

the cell is exposed to an agent that enhances permeability of the cell.

Claim 3 (original): The method of claim 1, wherein the nucleic acid molecule is greater than about 0.6 megabase.

Claim 4 (original): The method of claim 1, wherein the nucleic acid molecule is greater than about 1 megabase.

Claim 5 (original): The method of claim 1, wherein the nucleic acid molecule is greater than about 5 megabases.

Claim 6 (previously presented): The method of claim 1, wherein the nucleic acid molecule is a natural chromosome, an artificial chromosome, a fragment of a chromosome that is greater than about 0.6 megabase or naked DNA that is greater than about 0.6 megabase.

Claim 7 (original): The method of claim 1, wherein the nucleic acid molecule is an artificial chromosome.

Claim 8 (previously presented): The method of claim 1, wherein the nucleic acid molecule is an artificial chromosome expression system (Aces).

Claim 9 (original): The method of claim 1, wherein the nucleic acid molecule is exposed to the delivery agent *in vitro*, *ex vivo* or *in vivo*.

Claim 10 (original): The method of claim 1, wherein the contacting of the nucleic acid molecule that has been exposed to the delivery agent with the cell is effected *in vitro*, *ex vivo* or *in vivo*.

Claim 11 (original): The method of claim 1, wherein

exposure of the nucleic acid to a delivery agent is effected by mixing the nucleic acid with a delivery agent; and

the exposure of the cell to an agent that enhances permeability comprises applying ultrasound or electrical energy to the cell.

Claim 12 (original): The method of claim 1, wherein a delivery agent comprises a cationic compound.

Claim 13 (original): The method of claim 12, wherein the cationic compound is selected from the group consisting of a cationic lipid, a cationic polymer, a mixture of cationic lipids, a mixture of cationic polymers, a mixture of a cationic lipid and a cationic polymer, a mixture of a cationic lipid and a neutral lipid, polycationic lipids, non-liposomal forming lipids, activated dendrimers, and a pyridinium chloride surfactant.

Claim 14 (previously presented): The method of claim 12, wherein the delivery agent is a composition that comprises one or more cationic compounds, wherein the compound is selected from the group consisting of N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA), dioleoyl-phosphatidylethanolamine (DOPE), 2,3-dioleyloxy-N-[2(spermine-carboxamido)ethyl]-N,N-dimethyl-1-propanaminiumtrifluoroacetate (DOSPA), $C_{52}H_{106}N_6O_4 \cdot 4CF_3CO_2H$, $C_{88}H_{178}N_8O_4S_2.4CF_3CO_2H$, $C_{40}H_{84}NO_3P.CF_3CO_2H$,

$C_{50}H_{103}N_7O_3.4CF_3CO_2H$, $C_{55}H_{116}N_8O_2.6CF_3CO_2H$, $C_{49}H_{102}N_6O_3.4CF_3CO_2H$, $C_{44}H_{89}N_5O_3.2CF_3CO_2H$, $C_{100}H_{206}N_{12}O_4S_2.8CF_3CO_2H$, $C_{41}H_{78}NO_8P$) $C_{162}H_{330}N_{22}O_9.13CF_3CO_2H$, $C_{43}H_{88}N_4O_2.2CF_3CO_2H$, $C_{43}H_{88}N_4O_3.2CF_3CO_2H$, and (1-methyl-4-(1-octadec-9-enyl-nonadec-10-enylenyl) pyridinium chloride.

Claim 15 (original): The method of claim 1, wherein a delivery agent is energy.

Claim 16 (original): The method of claim 15, wherein the cell is treated with energy.

Claim 17 (original): The method of claim 15, wherein the energy is ultrasound energy.

Claim 18 (original): The method of claim 17, wherein the ultrasound energy is applied to the cell for about 30 seconds to about 5 minutes.

Claim 19 (original): The method of claim 17, wherein the ultrasound energy is applied as one continuous pulse.

Claim 20 (original): The method of claim 17, wherein the ultrasound energy is applied as two or more intermittent pulses.

Claim 21 (original): The method of claim 20, wherein the intermittent pulses of the ultrasound energy are applied for substantially the same length of time, at substantially the same energy level.

Claim 22 (original): The method of claim 20, wherein the intermittent pulses vary in energy level, the length of time applied, or energy level and the length of time applied.

Claim 23 (original): The method of claim 11, wherein prior to applying the ultrasound energy to the cell, the cell is contacted with a cavitation compound.

Claim 24 (original): The method of claim 17, wherein prior to applying the ultrasound energy to the cell, the cell is contacted with a cavitation compound

Claim 25 (original): The method of claim 11, wherein the agent that enhances permeability comprises applying electrical energy.

Claim 26 (original): The method of claim 1 that comprises:

(a) applying ultrasound or electrical energy to the cell; and

(b) contacting the cell, upon conclusion of the application of ultrasound or electrical energy, with a mixture of the nucleic acid molecule and a delivery agent, whereby the nucleic acid molecule is delivered into the cell.

Claim 27 (original): The method of claim 26, wherein the agent is a cationic compound.

Claim 28 (original): The method of claim 25, wherein the energy is ultrasound.

Claim 29 (original): The method of claim 28, wherein prior to applying the ultrasound energy, the cell is contacted with a cavitation compound.

Claim 30 (original): The method of claim 1 wherein the cell is a plant cell or an animal cell.

Claim 31 (original): The method of claim 1, wherein the cell is selected from the group consisting of a nuclear transfer donor cell, a stem cell,a primary cell, a cell from an immortalized cell line and a cell capable of the generation of a specific organ.

Claim 32 (original): The method of claim 1, wherein the cell is selected from the group consisting of a primary cell, an immortalized cell, an embryonic cell, a stem cell, a transformed cell and a tumor cell.

Claim 33 (original): The method of claim 1, wherein the cell is selected from the group consisting of a nuclear transfer donor cell, a stem cell, and a cell capable of the generation of a specific organ.

Claim 34 (original): A method for delivering a nucleic acid molecule into a cell comprising:

(a) contacting the cell in the absence of the nucleic acid molecule with a delivery agent, and applying ultrasound energy or electrical energy to the cell,

wherein the contacting and applying are performed sequentially or simultaneously; and then

(b) contacting the cell with the nucleic acid molecule, whereby the nucleic acid molecule is delivered into the cell.

Claim 35 (original): The method of claim 34, wherein the delivery agent comprises a cationic compound.

Claim 36 (previously presented): The method of claim 34, wherein the delivery agent is a composition that comprises one or more cationic compounds, wherein the compound is selected from the group consisting of N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA), dioleoyl-phosphatidylethanolamine (DOPE), 2,3-dioleyloxy-N-[2(spermine-carboxamido)ethyl]-N,N-dimethyl-1-propanaminiumtrifluoroacetate (DOSPA), $C_{52}H_{106}N_6O_4 \cdot 4CF_3CO_2H$, $C_{88}H_{178}N_8O_4S_2.4CF_3CO_2H$, $C_{40}H_{84}NO_3P.CF_3CO_2H$, $C_{50}H_{103}N_7O_3.4CF_3CO_2H$, $C_{55}H_{116}N_8O_2.6CF_3CO_2H$, $C_{49}H_{102}N_6O_3.4CF_3CO_2H$, $C_{44}H_{89}N_5O_3.2CF_3CO_2H$, $C_{100}H_{206}N_{12}O_4S_2.8CF_3CO_2H$, $C_{41}H_{78}NO_8P$), $C_{162}H_{330}N_{22}O_9.13CF_3CO_2H$, $C_{43}H_{88}N_4O_2.2CF_3CO_2H$, $C_{43}H_{88}N_4O_3.2CF_3CO_2H$, and (1-methyl-4-(1-octadec-9-enyl-nonadec-10-enylenyl) pyridinium chloride.

Claim 37 (original): The method of claim 34, wherein the delivery agent is 1-methyl-4-(1-octadec-9-enyl-nonadec-10-enylenyl) pyridinium chloride.

Claim 38 (original): The method of claim 34, wherein the nucleic acid molecule is greater than about 1 megabase.

Claim 39 (previously presented): The method of claim 34, wherein the nucleic acid molecule is selected from the group consisting of an artificial chromosome, a artificial chromosome expression system (ACes) and a natural chromosome or a fragment thereof that is greater than at least about 0.6 megabase.

Claim 40 (original): The method of claim 35, wherein the cationic compound is selected from the group consisting of a cationic lipid, a cationic polymer, a mixture of cationic lipids, a mixture of cationic polymers, a mixture

of a cationic lipid and a cationic polymer, a mixture of a cationic lipid and a neutral lipid, polycationic lipids, non-liposomal forming lipids, activated dendrimers and a pyridinium chloride surfactant.

Claim 41 (original): The method of claim 34, wherein the energy is ultrasound.

Claim 42 (previously presented): The method of claim 41, wherein the ultrasound energy is applied to the cell at between about 0.1 and 1 watt/cm^2, for about 30 seconds to about 5 minutes.

Claim 43 (original): The method of claim 41, wherein the ultrasound energy is applied as one continuous pulse or as two or more intermittent pulses.

Claim 44 (original): The method of claim 43, wherein:

the pulses are intermittent pulses; and

the intermittent pulses of the ultrasound energy are applied for substantially the same length of time, at substantially the same energy level.

Claim 45 (original): The method of claim 43, wherein:

the pulses are intermittent pulses; and

the intermittent pulses vary in energy level, the length of time applied, or energy level and the length of time applied.

Claim 46 (original): The method of claim 34, wherein prior to applying the

ultrasound energy, the cell is contacted with a cavitation compound.

Claim 47 (original): The method of claim 34, wherein the cell is selected from the group consisting of an embryonic stem cell, a nuclear transfer donor cell, a stem cell and a cell capable of the generation of a specific organ.

Claim 48 (original): A method for delivering nucleic acid molecule into a cell in a subject comprising:

(a) administering a delivery agent to the subject in the absence of the nucleic acid molecule;

(b) applying ultrasound or electrical energy to the subject after administering the agent; and

(c) administering nucleic acid molecule to the subject upon completion of the application of ultrasound or electrical energy, whereby the nucleic acid molecule is delivered into the cell.

Claim 49 (original): The method of claim 48, wherein the agent is a cationic compound.

Claim 50 (currently amended): The method of claim [48] 49, wherein administering the cationic compound and the nucleic acid molecule and applying the energy is directly to a localized region of the subject wherein the cell is present.

Claim 51 (previously presented): The method of claim 48, wherein the delivery agent is a composition that comprises one or more cationic compounds, wherein the compound is selected from the group consisting of N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA), dioleoyl-phosphatidylethanolamine (DOPE), 2,3-dioleyloxy-N-[2(spermine-carboxamido)ethyl]-N,N-dimethyl-1-propanaminiumtrifluoroacetate (DOSPA), $C_{52}H_{106}N_6O_4 \cdot 4CF_3CO_2H$, $C_{88}H_{178}N_8O_4S_2.4CF_3CO_2H$, $C_{40}H_{84}NO_3P.CF_3CO_2H$, $C_{50}H_{103}N_7O_3.4CF_3CO_2H$, $C_{55}H_{116}N_8O_2.6CF_3CO_2H$, $C_{49}H_{102}N_6O_3.4CF_3CO_2H$, $C_{44}H_{89}N_5O_3.2CF_3CO_2H$, $C_{100}H_{206}N_{12}O_4S_2.8CF_3CO_2H$, $C_{41}H_{78}NO_8P$), $C_{162}H_{330}N_{22}O_9.13CF_3CO_2H$, $C_{43}H_{88}N_4O_2.2CF_3CO_2H$, $C_{43}H_{88}N_4O_3.2CF_3CO_2H$, and (1-methyl-4-(1-octadec-9-enyl-nonadec-10-enylenyl) pyridinium chloride.

Claim 52 (original): The method of claim 50, wherein the region of the subject is selected from the group consisting of a joint, a tumor, an organ and a tissue.

Claim 53 (previously presented): The method of claim 48, wherein the nucleic acid molecule is greater than about 1 megabase.

Claim 54 (original): The method of claim 48, wherein the nucleic acid molecule is greater than about 5 megabases.

Claim 55 (original): The method of claim 48, wherein the nucleic acid molecule is selected from the group consisting of an artificial chromosome, a satellite artificial chromosome and a natural chromosome or a fragment thereof.

Claim 56 (original): The method of claim 49, wherein the cationic compound is selected from the group consisting of a cationic lipid, a cationic polymer, a mixture of cationic lipids, a mixture of cationic polymers, a mixture of a cationic lipid and a cationic polymer, a mixture of a cationic lipid and a neutral lipid, polycationic lipids, non-liposomal forming lipids, activated dendrimers and a pyridinium chloride surfactant.

Claim 57 (original): The method of claim 48, wherein the energy is ultrasound and prior to administering the ultrasound energy to the subject, the subject is administered a cavitation compound.

Claim 58 (Currently Cancelled)

Claim 59 (Currently Amended): A method for delivering a large nucleic acid molecule into a cell, comprising:

(a) contacting the nucleic acid molecule with a composition that comprises a cationic lipid, [The method of claim 58,] wherein: the cationic lipid composition comprises 2,3-dioleyloxy-N-[2(spermine-carboxamido)ethyl]-N,N-dimethyl-1-propanaminiumtrifluoroacetate (DOSPA) and dioleoylphosphatidyl-ethanolamine (DOPE); and the nucleic molecule is at least 5 megabases; and then

(b) contacting the nucleic acid molecule with a cell, wherein steps (a) and (b) are performed simultaneously or sequentially.

Claim 60 (Currently Cancelled)

Claim 61 (Currently Amended) The method of claim ~~58~~ 59, wherein the nucleic acid molecule is a natural chromosome, an artificial chromosome, a fragment of a chromosome, or naked DNA.

Claim 62 (Currently Amended) The method of claim ~~58~~ 59, wherein the cell is selected from the group consisting of a plant cell and an animal cell.

Claim 63 (Currently Amended) The method of claim ~~58~~ 59, wherein the cell is selected from the group consisting of a primary cell, an immortalized cell, an embryonic cell, a stem cell, a transformed cell and a tumor cell.

Claim 64 (Currently Amended) The method of claim ~~58~~ 59, wherein the nucleic acid molecule is contacted with the cell *in vitro*, *ex vivo* or *in vivo*.

Claim 65 (Currently Amended): A method for delivering a nucleic acid molecule into a cell in a subject comprising:

(a) mixing the nucleic acid molecule with a delivery agent; ~~and~~

(b) administering the mixture of nucleic acid molecule and agent to the subject; and

(c) applying ultrasound or electrical energy to the subject, whereby the nucleic acid molecule is delivered into the cell to a greater extent than using the agent or energy alone.

Claim 66 (original): The method of claim 65, wherein the agent is a cationic compound.

Claim 67 (previously presented): The method of claim 66, wherein the cationic
compound and the nucleic acid molecule mixture are applied locally.

Claim 68 (original): The method of claim 67, wherein the mixture is applied to a joint, a tumor, an organ or a tissue.

Claim 69 (original): The method of claim 65, wherein the nucleic acid molecule is greater than about 1 megabase.

Claim 70 (original): The method of claim 66, wherein the cationic compound is selected from the group consisting of a cationic lipid, a cationic polymer, a mixture of cationic lipids, a mixture of cationic polymers, a mixture of a cationic lipid and a cationic polymer, a mixture of a cationic lipid and a neutral lipid, polycationic lipids, non-liposomal forming lipids, activated dendrimers, and a pyridinium chloride surfactant.

Claim 71 (previously presented): The method of claim 65, wherein the nucleic acid molecule is selected from the group consisting of an artificial chromosome, an artificial chromosome expression system (ACes), a natural chromosome or a fragment thereof that is greater than at least about 0.6 megabase.

Claim 72 (original): The method of claim 65, wherein the nucleic acid molecule is a natural chromosome, an artificial chromosome, a fragment of a chromosome or naked DNA that is greater than at least about 0.6 megabase in size.

Claim 73 (original): A method for delivering nucleic acid molecule into a cell in a subject comprising:

(a) applying ultrasound or electrical energy to subject; and

(b) administering to the subject a nucleic acid molecule and a delivery agent, upon conclusion of the application of ultrasound or electrical energy, whereby the nucleic acid molecule is delivered into the cell, wherein the delivery agent and nucleic acid are administered sequentially or as a single composition.

Claim 74 (original): The method of claim 73, wherein the delivery agent is administered, upon conclusion of the application of ultrasound or electrical energy followed by administration of the nucleic acid molecule, whereby the nucleic acid molecule is delivered into a cell.

Claim 75 (original): The method of claim 73, wherein prior to applying the ultrasound energy, the subject is administered a cavitation compound.

Claim 76 (original): The method of claim 75, wherein the energy is ultrasound and prior to applying the ultrasound energy, the subject is administered a cavitation compound.

Claim 77 (original): The method of claim 63, wherein the agent is a cationic compound.

Claim 78 (original): The method of claim 77, wherein the cationic compound is selected from the group consisting of a cationic lipid, a cationic

polymer, a mixture of cationic lipids, a mixture of cationic polymers, a mixture of a cationic lipid and a cationic polymer, a mixture of a cationic lipid and a neutral lipid, polycationic lipids, non-liposomal forming lipids, activated dendrimers, and a pyridinium chloride surfactant.

Claim 79 (previously presented): The method of claim 73, wherein the delivery agent is a composition that comprises one or more cationic compounds, wherein the compound is selected from the group consisting of N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA), dioleoyl-phosphatidylethanolamine (DOPE), 2,3-dioleyloxy-N-[2(spermine-carboxamido)ethyl]-N,N-dimethyl-1-propanaminiumtrifluoroacetate (DOSPA), $C_{52}H_{106}N_6O_4 \cdot 4CF_3CO_2H$, $C_{88}H_{178}N_8O_4S_2.4CF_3CO_2H$, $C_{40}H_{84}NO_3P.CF_3CO_2H$, $C_{50}H_{103}N_7O_3.4CF_3CO_2H$, $C_{55}H_{116}N_8O_2.6CF_3CO_2H$, $C_{49}H_{102}N_6O_3.4CF_3CO_2H$, $C_{44}H_{89}N_5O_3.2CF_3CO_2H$, $C_{100}H_{206}N_{12}O_4S_2.8CF_3CO_2H$, $C_{41}H_{78}NO_8P$), $C_{162}H_{330}N_{22}O_9.13CF_3CO_2H$, $C_{43}H_{88}N_4O_2.2CF_3CO_2H$, $C_{43}H_{88}N_4O_3.2CF_3CO_2H$, and (1-methyl-4-(1-octadec-9-enyl-nonadec-10-enylenyl) pyridinium chloride.

Claim 80 (original): A method for delivering nucleic acid molecule into a cell in a subject comprising:

(a) applying ultrasound or electrical energy to the subject; and

(b) administering to the subject the nucleic acid molecule upon conclusion of the application of ultrasound or electrical energy, whereby the nucleic acid molecule is delivered into the cell.

Claim 81 (original): The method of claim 80, wherein the energy is ultrasound and prior to applying the ultrasound energy, the subject is administered a cavitation compound.

Claim 82 (original): The method of claim 80, wherein the agent comprises a cationic compound.

Claim 83 (original): The method of claim 80, wherein the nucleic acid molecule is a natural chromosome, an artificial chromosome, a fragment of a

chromosome or naked DNA that is greater than at least about 0.6 megabase in size.

Claims 84-138 (canceled)

Claim 140 (canceled)

Claim 141 (Currently Amended): ~~The kit of claim 140, further~~ A kit for delivering nucleic acids into cells, comprising:

a composition comprising an artificial chromosome;

a delivery agent that comprises a composition comprising a delivery agent;

reagents for performing sonoporation or electroporation; and

optionally instructions for delivering nucleic acids into cells.

Claim 142 (Original): The kit of claim 141, wherein the delivery agent comprises a compound is selected from the group consisting of a cationic lipid, a cationic polymer, a mixture of cationic lipids, a mixture of cationic polymers, a mixture of a cationic lipid and a cationic polymer, a mixture of a cationic lipid and a neutral lipid, polycationic lipids, non-liposomal forming lipids, activated dendrimers, and a pyridinium chloride surfactant.

143. (Previously Amended) The kit of claim 142, wherein the compound is selected from the group consisting of N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA), dioleoylphosphatidylethanolamine (DOPE), 2,3-dioleyloxy-N-[2(spermine-carboxamido)ethyl]-N,N-dimethyl-1-propanaminiumtrifluoroacetate (DOSPA), $C_{52}H_{106}N_6O_4{\cdot}4CF_3CO_2H$, $C_{88}H_{178}N_8O_4S_2{\cdot}4CF_3CO_2H$, $C_{40}H_{84}NO_3P{\cdot}CF_3CO_2H$, $C_{50}H_{103}N_7O_3{\cdot}4CF_3CO_2H$, $C_{55}H_{116}N_8O_2{\cdot}6CF_3CO_2H$, $C_{49}H_{102}N_6O_3{\cdot}4CF_3CO_2H$, $C_{44}H_{89}N_5O_3{\cdot}2CF_3CO_2H$, $C_{41}H_{78}NO_8P$), $C_{100}H_{206}N_{12}O_4S_2{\cdot}8CF_3CO_2H$, $C_{162}H_{330}N_{22}O_9{\cdot}13CF_3CO_2H$, $C_{43}H_{88}N_4O_2{\cdot}2CF_3CO_2H$, $C_{43}H_{88}N_4O_3{\cdot}2CF_3CO_2H$ and (1-methyl-4-(1-octadec-9-enyl-nonadec-10-enylenyl) pyridinium chloride.

Claim 144 (new): The method of claim 1, wherein the nucleic acid molecule is about 10 megabases to about 450 megabases.

Claim 145 (new): The method of claim 1, wherein the nucleic acid molecule is about 90 megabases to about 120 megabases.

Claim 146 (new): The method of claim 1, wherein the nucleic acid molecule is about 15 megabases to about 50 megabases.

Claim 147 (new): The method of claim 59, wherein the nucleic acid molecule is about 10 megabases to about 450 megabases.